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**SUPPLEMENTAL INFORMATION DISCLOSURE  
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**ATTY. DOCKET NO.**  
GC541-3-D1  
Previously 23623-7076

**SERIAL NO.**  
10/062,970

**APPLICANT**  
Jones et al.

**FILING DATE**  
February 1, 2002

**GROUP ART UNIT**  
1623

**REFERENCE DESIGNATION**

**U.S. PATENT DOCUMENTS**

EXAM'R INITIAL		DOCUMENT NUMBER	DATE	NAME	Class	Subclass	Filing Date If Appropriate
	A1	*5,403,737	04/04/95	Abrahmsen et al.			
	A2	*5,629,173	05/13/97	Abrahmsen et al.			
	A3	*5,316,935	05/31/94	Arnold et al.			
	A4	*5,208,158	05/04/93	Bech et al.			
	A5	*5,244,791	09/14/93	Estell			
	A6	*5,316,941	05/31/94	Estell et al.			
	A7	*5,955,340	02/21/99	Bott			
	A8	*5,340,735	08/23/94	Christiansen et al.			

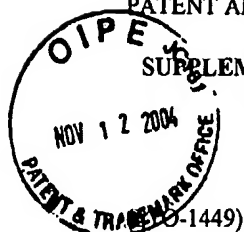
**FOREIGN PATENT DOCUMENTS**

EXAM'R INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	Subclass	TRANSLAT'N
LCM	B1	EP 0 328 229 A1	08/16/89	EP			
	B2	*WO 00/01742	01/13/00	PCT			
LCM	B3	WO 91/16423	04/18/91	PCT			
LCM	B4	WO 96/27671	02/27/96	PCT			
LCM	B5	WO 97/37007	10/09/97	PCT			
LCM	B6	WO 98/23732	06/04/98	PCT			
LCM	B7	WO 99/20723	04/29/99	PCT			
LCM	B8	WO 99/37323	07/29/99	PCT			
LCM	B9	WO 99/37324	07/29/99	PCT			

**OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)**

LCM	C1	Bech et al., "Chemical Modifications of a Cysteiny Residue Introduced in the Binding Site of Carboxypeptidase Y by Site-Directed Mutagenesis," <u>Carlsberg Res. Commun.</u> , 53:381-393 (1988)
LCM	C2	Bech et al., "Significance of Hydrophobic S <sub>4</sub> -P <sub>4</sub> Interactions in Subtilisin 309 from <i>Bacillus lentus</i> ," <u>Biochemistry</u> , 32:2847-2852 (1993)
LCM	C3	Berglund et al., "Altering the Specificity of Subtilisin <i>B. Lentus</i> by Combining Site-Directed Mutagenesis and Chemical Modification," <u>Bioorganic &amp; Mechanical Chemistry Letters</u> , 6:2507-2512 (1996)
	C4	*Berglund et al., "Chemical Modification of Cysteine Mutants of Subtilisin <i>Bacillus Lentus</i> Can Create Better Catalysts Than The Wild-Type Enzyme," <u>J. Am. Chem. Soc.</u> , 119:5265-5266 (1997)

EXAMINER Lugh C. Maur DATE CONSIDERED 12-14-04  
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LCM	C6	Bonneau et al., "Alteration of the Specificity of Subtilisin BPN' by Site-Directed Mutagenesis in its S <sub>1</sub> and S <sub>1</sub> ' Binding Sites," <i>J. Am. Chem. Soc.</i> , 113:1026-30 (1991)
LCM	C7	Brocklehurst, "Specific Covalent Modification of Thiols: Applications in the Study of Enzymes and Other Biomolecules," <i>Int. J. Biochem.</i> , 10:259-274 (1979)
LCM	C8	Bruice et al., "Novel Alkyl Alkanethiolsulfonate Sulfhydryl Reagents. Modification of Derivatives of L-Cysteine," <i>Journal of Protein Chemistry</i> , 1:47-58 (1982)
LCM	C9	Chen et al., "Probing the S-1' Subsite Selectivity of an Industrial Alkaline Protease in Anhydrous t-Butanol," <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 3(4):727-33 (1993)
LCM	C10	Davies et al., "A Semisynthetic Metalloenzyme Based on a Protein Cavity That Catalyzes the Enantioselective Hydrolysis of Ester and Amide Substrates," <i>J. Am. Chem. Soc.</i> , 119:11643-11652 (1997)
LCM	C11	Davis, B.G., et al., "Altering the specificity of subtilisin <i>Bacillus lentus</i> through the introduction of positive charge at single amino acid sites," <i>Bioorganic and Medicinal Chemistry</i> , (1999 Nov.) 7 (11) 2303-11, XPO000892841
LCM	C12	Davis, B.G., et al., "Controlled site selective protein glycosylation for precise glycan structure catalytic activity relationships," <i>Bioorganic &amp; Medicinal Chemistry</i> , Vol. 8, 2000, pp. 1527-1535
LCM	C13	Davis, B.G., et al., "Glycomethanethiosulfonates: powerful reagents for protein glycosylation," <i>Tetrahedron: Asymmetry</i> , NL, Elsevier Science Publishers, Amsterdam, Vol 11, No. 1, January 2000 (2000-01), pp. 245-262
LCM	C14	Davis, B.G., et al., "The controlled introduction of multiple negative charge at single amino acid sites in subtilisin <i>Bacillus lentus</i> ," <i>Bioorganic and Medicinal Chemistry</i> , (1999 Nov.) 7 (11) 2293-301, XPO000892840
DUP	C15	*Davis, Benjamin G, et al., "Controlled Site Selective Glycosylation of Proteins by a Combined Site Directed Mutagenesis and Chemical Modification Approach," <i>J. Org. Chem.</i> , Vol. 63, January 12, 1998 (1998-01-12), pp. 9614-9615
LCM	C16	DeSantis et al., "Chemical Modifications at a Single Site Can Induce Significant Shifts in the pH Profiles of a Serine Protease," <i>J. Am Chem. Soc.</i> , 120:8582-8586 (1998)
LCM	C17	Desantis, G., et al, "Probing the altered specificity and catalytic properties of mutant subtilisin chemically modified at position S156C and S166C in the S1 pocket," <i>Bioorganic and Medicinal Chemistry</i> , (1997) 7/7 (1381-1387), XP0000892843
DUP	C18	*DeSantis, G., et al., "Site-Directed Mutagenesis Combined with Chemical Modification As a Strategy for Altering the Specificity of the S1 and S1' Pockets of Subtilisin <i>Bacillus Lentus</i> ," <i>Biochemistry</i> (1998) 37 (17) 5968-73
LCM	C19	Dickman, M., et al., "Chemically modified mutants of subtilisin <i>Bacillus lentus</i> catalyze transesterification reactions better than wild type," <i>Tetrahedron Asymmetry</i> , (11. Dec. 1998) 9/23 4099-4102, XPO000901276.

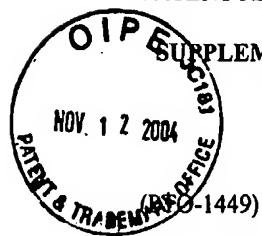
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*Lugh C. Maier*

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LCM	C20	Gron et al., "A Highly Active and Oxidation-Resistant Subtilisin-Like Enzyme Produced by a Combination of Site-Directed Mutagenesis and Chemical Modification," <u>Eur. J. Biochem.</u> , 194:897-901 (1990)
LCM	C21	Kaiser, "Catalytic Activity of Enzymes Altered at Their Active Sites," <u>Agnew. Chem. Int. Ed. Engl.</u> , 27:913-922 (1988)
LCM	C22	Kawase et al., "Effect of Chemical Modification of Tyrosine Residues on Activities of Bacterial Lipase," <u>Journal of Fermentation and Bioengineering</u> , 72:317-319 (1991)
LCM	C23	Kenyon et al., "Novel Sulfhydryl Reagents," <u>Methods Enzymol.</u> , 47:407-430 (1977)
LCM	C24	Kluger et al., "Amino Group Reactions of the Sulfhydryl Reagent Methyl Methanesulfonylthioate. Inactivation of D-3-hydroxybutyrate Dehydrogenase and Reaction with Amines in Water," <u>Can. J. Biochem.</u> , 58:629-632 (1980)
LCM	C25	Lloyd, R.C. et al., "Site Selective Glycosilation of Subtilisin Bacillus Lentus Causes Dramatic Increase in Esterase Activity," <u>Biorganic &amp; Medicinal Chemistry</u> , Vol. 8, 2000, pp. 1537-1544
LCM	C26	Lo, Bryan, et al., "Replacement of Ala-166 with Cysteine in the High Affinity Rabbit Sodium Glucose Transporter Alters Transport Kinetics and Allows Methanethiosulfonate Ethylamine to Inhibit Transporter Function," <u>The Journal of Biological Chemistry</u> , 273:2 903-909 (1998)
LCM	C27	Neet, K.E. and Koshland, D.E., "The Conversion of Serine at the Active Site of Subtilisin to Cysteine: A 'Chemical Mutation,'" <u>Proc. Nat. Acad. Sci. USA</u> , 56(5):1606-1611.
LCM	C28	Nishimura et al., "Reversible Modification of the Sulfhydryl Groups of <i>Escherichia coli</i> Succinic Thiokinase with Methanethiolating Reagents, 5,5'-Dithio-bis(2-Nitrobenzoic Acid), p-Hydroxymercuribenzoate, and Ethylmercurithiosalicylate," <u>Archives of Biochemistry and Biophysics</u> , 170:461-467 (1975)
LCM	C29	Paulson, J.C., "Glycoproteins: what are the sugar chains for?" <u>TIBS</u> , 14:272-276 (1989)
LCM	C30	Planas et al., "Reengineering the Catalytic Lysine of Aspartate Aminotransferase by Chemical Elaboration of a Genetically Introduced Cysteine," <u>Biochemistry</u> , 30:8268-8276 (1991)
LCM	C31	Plettner, E., et al., "Modulation of Esterase and Amidase Activity of Subtilisin Bacillus Lentus by Chemical Modification of Cysteine Mutants," <u>Journal of the American Chemical Society</u> , (2 Jun. 1999) 121/21, 4977-4981, XPO000891274.
LCM	C32	Plettner, Erika et al., "A Combination Approach to Chemical Modification of Subtilisin Bacillus Lentus," <u>Biorganic &amp; Medicinal Chemistry Letters</u> (Sept. 8, 1998) Vol. 8, No. 17, pp. 2291-2296, XP0004138220
LCM	C33	Polgar et al., "A New Enzyme Containing a Synthetically Formed Active Site. Thiol-Subtilisin," <u>Journal of American Chemical Society</u> , 88:3153-3154 (1966)
LCM	C34	Ramachandran et al., "Stabilization of Barstar by Chemical Modification of the Buried Cysteines," <u>Biochemistry</u> , 35:8776-8785 (1996)
LCM	C35	Roberts et al., "Reactivity of Small Thiolate Anions and Cysteine-25 in Papain Toward Methyl Methanethiosulfonate," <u>Biochemistry</u> , 25:5595-5601 (1986)

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LCM	C36	Siddiqui et al, "Arthrobacter D-Xylose Isomerase: Chemical Modification of Carboxy Groups and Protein Engineering Of pH Optimum," <u>Biochem. J.</u> , 295:685-691 (1993)
LCM	C37	Smith et al., "An Engineered Change in Substrate Specificity of Ribulosebiphosphate Carboxylase/Oxygenase," <u>The Journal of Biological Chemistry</u> , 265:1243-1245 (1990)
LCM	C38	Smith et al., "Chemical Modification of Active Site Residues in $\gamma$ -Glutamyl Transpeptidase," <u>The Journal of Biological Chemistry</u> , 270:12476-12480 (1995)
LCM	C39	Smith et al., "Restoration of Activity to Catalytically Deficient Mutants of Ribulosebiphosphate Carboxylase/Oxygenase by Aminoethylation," <u>The Journal of Biological Chemistry</u> , 263:4921-4925 (1988)
LCM	C40	Smith et al., "Simple Alkanethiol Groups for Temporary Blocking of Sulfhydryl Groups of Enzymes," <u>Biochemistry</u> , 14:766-771 (1975)
LCM	C41	Smith et al., "Subtle Alteration of the Active Site of Ribulose Bisphosphate Carboxylase/Oxygenase by Concerted Site-Directed Mutagenesis and Chemical Modification," <u>Biochemical and Biophysical Research Communications</u> , 152:579-584 (1988)
LCM	C42	Spura, A., et al. "Probing Agonist Domain of the Nicotinic Acetylcholine Receptor by Cysteine Scanning Mutogenesis Reveals Residues in Proximity to the Alpha-Bungarotoxin Binding Site," <u>Biochemistry</u> , 20 Apr. 1999 Vol. 38:16 pp. 4912-4921
LCM	C43	Stewart et al., "Catalytic Oxidation of Dithiols by a Semisynthetic Enzyme," <u>J. Am. Chem. Soc.</u> , 108:3480-3483 (1986)
LCM	C44	Valenzuela et al., "Kinetic Properties of Succinylated and Ethylenediamine-Amidated $\delta$ -Chymotrypsins," <u>Biochim. Biophys. Acta</u> , 250:538-548 (1971)
LCM	C45	West et al., "Enzymes as Synthetic Catalysts: Mechanistic and Active-Site Considerations of Natural and Modified Chymotrypsin," <u>J. Am. Chem. Soc.</u> , 112:5313-5320 (1990)
LCM	C46	White et al., "Sequential Site-Directed Mutagenesis and Chemical Modification to Convert the Active Site Arginine 292 Of Aspartate Aminotransferase to Homoarginine," <u>Journal of the American Chemical Society</u> , 114:292-293 (1992)
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LCM	C48	Wynn et al., "Comparison of Straight Chain and Cyclic Unnatural Amino Acids Embedded in the Core of Staphylococcal Nuclease," <u>Protein Science</u> , 6:1621-1626 (1997)
LCM	C49	Wynn et al., "Mobile Unnatural Amino Acid Side Chains in the Core of Staphylococcal Nuclease," <u>Protein Science</u> , 5:1026-1031 (1996)
LCM	C50	Wynn et al., "Unnatural Amino Acid Packing Mutants of <i>Escherichia Coli</i> Thioredoxin Produced by Combined Mutagenesis/Chemical Modification Techniques," <u>Protein Science</u> , 2:395-403 (1993)

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